

REMARKS

After entry of this amendment, claims 1-16, 18-77, and 113-140 are pending. Claims 27-35, 48-77, and 113-140 are withdrawn as directed to nonelected subject matter. Claims 6, 8, 10, 12-16, 18-26, 42-44, 46 and 47 read on the elected species; claims 1-5, 7, 9, 11, 36-41 and 45 are withdrawn as directed to unelected species. Claim 12 is amended and claim 17 is canceled. The amended claim is supported in the specification by, for example, paragraphs [0041] and [0042].

The Claimed Invention

In this case, claim 6 requires the elements of (1) an electron conductor, (2) an enzyme capable of reacting with an oxidized form of an electron mediator and a fuel fluid to produce an oxidized form of the fuel fluid and a reduced form of the electron mediator, (3) the reduced form of the electron mediator being capable of releasing electrons to the electron conductor, (4) an enzyme immobilization material immobilizing and stabilizing the enzyme, (5) the enzyme immobilization material being permeable to the fuel fluid, and (6) the stabilized enzyme retaining at least about 75% of its initial catalytic activity for at least about 30 days.

Obviousness-type Double Patenting

Reconsideration is respectfully requested of the provisional rejection of claims 6, 8, 10, 12-26, 42-44, 46, and 47 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-15, 22, 40-44, and 48 of copending Application No. 10/931,147. The analysis employed in an obvious-type double patenting rejection parallels the guidelines of a 35 U.S.C. § 103 obviousness determination.¹ However, an important distinction exists. A rejection for obviousness must be based on a comparison of the claimed invention to the entirety of the disclosure in the prior art reference, whereas an obviousness-type double patenting rejection must be grounded on a comparison of the claimed invention to the claims, **and only the claims**, of the reference.²

¹ *In re Braat*, 937 F.2d 589 (Fed. Cir. 1991).

² *Purdue Pharma L.P. v. Boehringer Ingelheim GmbH*, 98 F.Supp.2d 362, 392, 55 USPQ2d 1168, 1190 (S.D.N.Y. 2000), *aff'd*, 237 F.3d 1359, 57 USPQ2d 1647 (Fed. Cir. 2001).

It is respectfully submitted that the subject matter of the claims of the present application would not have been obvious in view of the claims of copending Application No. 10/931,147. When evaluating the scope of a claim, every element of the claim must be considered.³ To support an obviousness-type double patenting rejection, the claims must have been obvious at the time of filing and not merely obvious upon hindsight reconstruction using applicant's disclosure as a template to arrive at the features of the instantly claimed bioanodes from the claims of the '147 application. It is respectfully submitted that the Office has failed to establish obviousness based on any reference or by evidence of the level of skill in the art or the nature of the problem that is not based upon impermissible hindsight reconstruction.

In particular, claim 6 requires an enzyme capable of reacting with an oxidized form of an electron mediator and a fuel fluid to produce an oxidized form of the fuel fluid and a reduced form of the electron mediator that would not have been obvious from the claims of the '147 application; the enzymes used in the bioanode and biocathode of the biofuel cell are different and as such have different reduction potentials. Due to these differences, various electrode elements are selected to prepare electrodes having advantageous electron transfer characteristics. One of these selections in the instant application was the use of an electron mediator wherein its reduced form is capable of releasing electrons to the electron conductor. This would not have been an obvious variant of the claims of the '147 application, and thus, claims 6, 8, 10, 12-26, 42-44, 46, and 47 are patentable over claims 1-15, 22, 40-44, and 48 of copending Application No. 10/931,147.

35 U.S.C. § 112

Reconsideration is respectfully requested of the rejection of claims 12 and 17 under 35 U.S.C. § 112, second paragraph, as being indefinite. Without conceding the propriety of the rejection and to expedite prosecution, claim 12 has been amended to require the perfluoro sulfonic acid-PTFE copolymer is "modified with a hydrophobic cation larger than NH_4^+ wherein the hydrophobic cation exchanges for protons as the counterion to the $-\text{SO}_3^-$ groups of the perfluoro sulfonic acid-PTFE copolymer." Thus, a person of skill in the art would know exactly what the modification is without resort to the

³ See, e.g., In re Ochiai, 71 F.3d 1565, 1572, 37 USPQ2d 1127, 1133 (Fed. Cir. 1995).

specification. Claim 17 has been canceled, so the rejection is moot with respect to claim 17. Thus, claim 12 satisfies the definiteness requirement of 35 U.S.C. § 112, second paragraph.

35 U.S.C. § 103 Rejections

There are three criteria for establishing a *prima facie* case of obviousness.

First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach all or suggest all the claim limitations.⁴

Further, as noted in M.P.E.P. §2112.IV, an obviousness rejection based upon the inherency of a claimed element must be supported by evidence that the missing element is necessarily present in the references, and that it would be so recognized by one skilled in the art:

The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art); *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' " *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted). . . .

"In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original) (Applicant's invention was directed to a biaxially oriented, flexible dilation catheter balloon (a tube which expands upon inflation) used, for example, in clearing the blood vessels of heart patients). The examiner applied a U.S. patent to Schjeldahl which disclosed injection molding a tubular

⁴ See M.P.E.P. § 2143.

preform and then injecting air into the preform to expand it against a mold (blow molding). The reference did not directly state that the end product balloon was biaxially oriented. It did disclose that the balloon was "formed from a thin flexible inelastic, high tensile strength, biaxially oriented synthetic plastic material." *Id.* at 1462 (emphasis in original). The examiner argued that Schjeldahl's balloon was inherently biaxially oriented. The Board reversed on the basis that the examiner did not provide objective evidence or cogent technical reasoning to support the conclusion of inherency.).

1. Karyakin et al.

Reconsideration is respectfully requested of the rejection of claims 6, 8, 10, 12, 42-44, and 47 under 35 U.S.C. § 103 as being unpatentable over Karyakin et al., *Anal. Chem.* **1996**, 68, 4335-4341. Karyakin et al. describe an enzyme-Nafion® complex made by mixing an enzyme suspension (e.g., glucose oxidase or alcohol dehydrogenase) with Nafion® solution in 85% ethanol in water. The focus of the reference was providing a uniform Nafion® layer. A uniform Nafion® layer was not obtained when an aqueous solution (or aqueous buffer solution) was used to suspend the Nafion®.

The Examiner asserts that "coasting of Nafion® and the enzyme allows for stabilization of the enzymes."⁵ However, the data in Example 1 of the specification shows that unmodified Nafion® does not stabilize alcohol dehydrogenase, aldehyde dehydrogenase, formate dehydrogenase, glucose dehydrogenase, lactic dehydrogenase, or formaldehyde dehydrogenase. Further, as demonstrated in the attached declaration from Dr. Shelley Minter, inventor of the subject application, glucose oxidase has a much lower activity when cocast in unmodified Nafion® than when dispersed in buffer.

Further, Karyakin et al. do not report stability of the electrodes, and one skilled in the art would have had to have recognized such stability in order for the Office to take the position that stability is inherent in the Karyakin reference. Therefore, the stability requirement of claim 6 is not met or suggested by the Karyakin reference and claims 6, 8, 10, 12, 42-44, and 47 are not obvious in view of the cited reference.

⁵ Page 4 of Office action dated December 10, 2007.

2. Karyakin et al. in view of Jin

Reconsideration is respectfully requested of the rejection of claims 17-22 under 35 U.S.C. § 103 as being unpatentable over Karyakin et al., *Anal. Chem.* **1996**, 68, 4335-4341 in view of Jin, *Mikrochim. Acta* **1993**, 112, 71-75. The Karyakin reference is discussed in more detail above. Jin describes electrodes prepared by coating Nafion® on a glassy carbon electrode and drying. Then, the Nafion® coated electrode was immersed in methyl viologen for 20 minutes, followed by rinsing with distilled water. Then, a mixture of uricase, bovine serum albumin, and glutaraldehyde in citric acid-dibasic sodium phosphate buffer was spread on the surface of the methyl viologen-Nafion® modified electrode and allowed to dry. In this mixture, uricase is an enzyme, glutaraldehyde crosslinks the uricase to the Nafion® layer, and the bovine serum albumin stabilizes the uricase. In sum, this procedure of drying the Nafion® on the glassy carbon electrode followed by immersion of the electrode in methyl viologen would have allowed only a portion of the protons attached to the -SO₃⁻ sites of the Nafion® to exchange for methyl viologen, and because the Nafion® was dried prior to contact with methyl viologen and the uricase enzyme was crosslinked to the Nafion® layer, the pore structure of the dried Nafion® would not have been altered in a way that would have stabilized the uricase.

Further, Jin describes the enzyme in the electrode as active for 14 days if stored in the refrigerator. However, activity gradually wanes with the increase of measurement time, for example, the response value decreases by 3.7% for every 50 measurements. Since the response time for each measurement is approximately 25 seconds (see figure 1, page 73), 50 measurements would take about 20.8 minutes and a degradation of response value by 25% to 75% of the initial response would take about 140.8 minutes (2.35 hours). Consequently, the stability requirement of claims 18-22 is not met or suggested by the Jin reference. Further, as described above, the Karyakin reference does not meet the stability requirement of claims 18-22 and the Jin reference does not remedy the deficiency of the Karayakin reference. Claim 17 is canceled, so the rejection is moot with respect to claim 17. Therefore, claims 18-22 are not obvious in view of the cited references.

3. Zawodzinski et al. in view of Gregg et al.

Reconsideration is requested of the rejection of claims 6, 13-16, and 23-26 as being unpatentable over Zawodzinski et al., *Electroanalysis* **1995**, 7(11), 1035-1040 in view of Gregg (U.S. Patent No. 5,264,105). Zawodzinski et al. describe glucose sensors that have glucose oxidase, Nafion[®], and carbon-supported platinum on glassy carbon or carbon cloth electrodes. Figure 7 on page 1039 shows the electrodes retain roughly 90% of their activity over the course of 200 days with storage in phosphate buffer solution at 4°C between runs. The figure implies that 13 discrete current measurements were made over the course of 200 days. Since each measurement takes on the order of minutes to complete, the total time that the enzyme is reacting with the analyte is from 2-13 hours, when estimating each measurement takes 10-60 minutes to perform. Thus, the stability requirement of claim 6 is not met or suggested by the Zawodzinski reference.

Gregg et al. describe electrodes containing enzymes that are immobilized within redox polymers with optional overcoatings of Nafion[®]. However, Gregg et al. are silent with regard to the stability of these enzymes within the electrodes. Thus, the Gregg et al. reference *does not explicitly disclose* enzymes stabilized by enzyme immobilization materials wherein the enzyme retains at least about 75% of its initial catalytic activity for at least about 30 days, and the rejection is based on the inherency of stabilized enzymes while continuously reacting with the electron mediator. No evidence or technical reasoning has been provided by the Office as to why one skilled in the art would have recognized that such enzyme stability is necessarily present in the Gregg et al. reference. Inherency cannot be established by mere possibilities. Absent such evidence or reasoning, applicants submit that a proper prima facie case of obviousness has not been established, and the burden of proof has not shifted to applicants.

Whether or not a person of skill in the art would have substituted Zawodzinski's platinum with Gregg's osmium²⁺(2,2'-bipyridine)₃ for the benefit of providing fast chemical reaction of the analyte,⁶ neither Gregg nor Zawodzinski, alone or in combination disclose the stability requirement of claim 6. Thus, claims 6, 13-16, and 23-26 are patentable over Zawodzinski et al. in view of Gregg et al.

⁶ Pages 6-7 of the Office action dated December 10, 2007.

4. Zawodzinski et al. in view of Gregg et al. and further in view of Khan

It appears that this rejection refers to the elements of a biocathode, particularly the elements of the biocathode claimed in copending Application No. 10/931,147. Thus, if this rejection is to be maintained in a subsequent action, clarity with respect to the application of the references to the elements of the bioanode of claim 6 would be needed. In any event, the claims are patentable over Zawodzinski et al., *Electroanalysis* **1995**, 7(11), 1035-1040 in view of Gregg (U.S. Patent No. 5,264,105) and further in view of Khan (US 2004/0217016). The deficiencies of Zawodzinski et al. and Gregg et al. with respect to the requirements of claim 6 are detailed above.

Khan generally discloses electrochemical test strips and methods for analyte detection. The disclosure of Khan generally describes enzymes and mediators used in the test strips and discloses that enzymes are selected depending on the analyte to be detected. The enzymes work to oxidize the analyte of interest. Khan does not disclose enzyme immobilization materials or describe the stability of the enzymes in the test strips.

The Office is taking the position that it would have been obvious to substitute the enzymes and electron mediators of Zawodzinski's electrode with those disclosed in Khan. However, neither Zawodzinski nor Khan suggests such a substitution. Regardless of whether one skilled in the art would have been motivated to make such a substitution, the combination of Khan with Zawodzinski et al. and Gregg et al. does not overcome the deficiencies of the combination of Zawodzinski et al. and Gregg et al. with respect to the enzyme stability requirement of claim 6 and the claims that depend therefrom. Khan does not disclose an enzyme immobilization material at all and therefore does not address the deficiency of the Zawodzinski et al. and Gregg et al. references regarding enzyme stability. Thus, a person skilled in the art would not have contemplated combining the teachings of Zawodzinski et al., Gregg et al., and Khan to arrive at the bioanodes of the claims nor would the combined references have provided a reasonable expectation that an immobilized enzyme in the bioanode would retain at least about 75% of its initial catalytic activity for at least about 30 days while continuously reacting with the electron mediator.

Moreover, the Office is engaged in impermissible hindsight using the applicant's claims as a template. The references or particular teachings of the references cannot

be treated in isolation. When taken as a whole, the cited references would not have led a skilled artisan to develop the claimed biocathodes without using the applicant's disclosure as well. Thus, the pending claims are patentable over the cited references.

Rejoinder

Pursuant to M.P.E.P. §821.04, Applicants again request rejoinder of withdrawn claims 27-35, 49-52, 60-62, 114, and 117-130 as they depend from claim 6 and therefore require all the limitations of claim 6. Applicants further request reconsideration of withdrawn unelected species claims 1-5, 7, 9, 11, 36-41, and 45 because they either require all the limitations of claim 6 or overlap the scope of claim 6.

CONCLUSION

Applicant submits that the present application is in condition for allowance and requests early allowance of the pending claims.

The Commissioner is hereby authorized to charge any under payment or credit any over payment to Deposit Account No. 19-1345.

Respectfully submitted,

A handwritten signature in black ink, reading "Janet S. Hendrickson". The signature is fluid and cursive, with a long horizontal flourish extending to the right.

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